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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

A3

WO 00/48583

(54) Title: FORMULATION OF 5-HT AGONISTS WITH NSAIDS, ESPECIALLY COX-2 INHIBITORS, FOR TREATING MIGRAINE

(57) Abstract: This invention comprises a method of treating migraine in a human comprising co-timely administering of a therapeutically effective amount of a 5-HT agonist coordinated with a therapeutically effective amount of an NSAID, particularly a long-acting NSAID, and particularly of the class of NSAIDs termed cyclooxygenase-2 inhibitors (COX-2 inhibitors) such as celecoxib (Celebrex[®]), rofecoxib (Vioxx[®]), meloxicam, piroxicam, JTE-522, L-745,337, and NS398, and in some instances, doses below those ordinarily considered as minimum effective doses as to one or both 5-HT agonist and long-acting NSAID. Dosage forms are included herein.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/03897

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 20870 A (POZEN INC) 22 May 1998 (1998-05-22) page 12, line 10-18; claims 5-7,20-28 page 19, line 8 -page 23, line 19 page 23, line 20 -page 24, line 5 ----	1,2, 21-23, 29-33
X	PAVEL AND BALUCH: "Formulation of Antimigraine Mixtures" STN HCA,XX,XX, vol. 8, no. 121, 22 August 1994 (1994-08-22), XP002078672 the whole document ----	1,5,21, 22,29, 31,32
A		2,33,35
X	HAAG: "Kombianalgetika in der Kopfschmerztherapie" DEUTSCHE APOTHEKER ZEITUNG,DE,DEUTSCHER APOTHEKER ZEITUNG, STUTTGART, vol. 4, no. 138, 22 January 1998 (1998-01-22), pages 43-48, XP002079370 ISSN: 0011-9857 table 1 ----	1,5,21, 22
X	GB 2 135 884 A (SANDOZ LTD) 12 September 1984 (1984-09-12) claims 1,15-18 ----	1,5,21, 22,29, 31,32 2,33,35
A	DE 195 42 281 A (BOEHRINGER INGELHEIM KG) 15 May 1997 (1997-05-15) claims 5,6,8 ----	1,2
A	WO 97 38986 A (SEARLE & CO) 23 October 1997 (1997-10-23) page 5, line 7-9 page 4, line 22-26 ----	1,2

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-23 and 25-38 relate to methods and compositions involving compounds defined by reference to desirable characteristics or properties, namely agonism of the 5-HT receptor, analgesic activity, anti-inflammatory activity, inhibition of COX-2, and establishing certain peak blood- or blood plasma levels of an (unspecified) compound. The claims cover all compounds having these characteristics or properties, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT - for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). A compound cannot be sufficiently defined by its mechanism of action and/or its pharmacological profile. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Furthermore, the claims relate to an extremely large number of possible compositions and methods by means of the above expressions, as well as terms like "sub-MED amounts", "long-acting", "co-timely", and "about". The term "non-Non Steroidal Anti Inflammatory Drug" is confusing, as it should be taken to mean "Steroidal AID", which would render claims 31 and 32, and page 2, lines 30-31 of the description, contradictory. This term was read as "non-steroidal, non-opiate anti-inflammatory drug possibly not listed as anti-inflammatory".

The term "sub-MED amounts" (claims 26-28) is not sufficiently defined on page 7, lines 26-31, especially in view of the definition of "therapeutically effective amount" (page 9, under "B") which is used in independent claim 1, upon which claims 26-28 depend. Besides, page 7 does not define "sub-MED" amounts for all possible 5-HT agonists and (non-) NSAID analgesics.

The term "long-acting" (claim 35), although defined for some NSAIDs on page 8, under "A", does not specify the meaning of this term in relation to COX-2 inhibitors in general and in relation to celecoxib in particular.

The term "co-timely" (claims 29,33) is not sufficiently defined on page 15, under "C", lines 9-10.

Due to the above, a lack of clarity (and/or conciseness) within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the complete scope of the claims impossible.

Finally, the scope of claim 20 is not readily identifiable because of the wording: "less than about from about...".

Consequently, the search has been carried out for those parts of the claims which appear to be clear, concise, supported and disclosed, namely those parts relating to the specific compounds, compositions and methods referred to in present claims 3-20, 22-24, 30-32, 34 and 36-40, and disclosed in the examples, with due regard to the description and to the general idea underlying the application.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims 24, 39 and 40 have been completely searched.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/03897

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
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DE 19542281	A 15-05-1997	AU AU BG BG BR CA CN CZ WO EP HU JP NO PL SK US	706112 B 7623096 A 62511 B 102408 A 9611502 A 2232008 A 1202111 A 9801498 A 9717971 A 0861081 A 9903489 A 2000500446 T 982172 A 326653 A 61398 A 5942503 A	10-06-1999 05-06-1997 31-01-2000 30-12-1998 02-03-1999 22-05-1997 16-12-1998 14-10-1998 22-05-1997 02-09-1998 28-03-2000 18-01-2000 13-05-1998 12-10-1998 09-09-1998 24-08-1999

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61P25/06 A61K45/06 A61K31/415

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category ^a	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 00 25779 A (MERCK & CO INC) 11 May 2000 (2000-05-11) page 4, line 9-19; claims 1-9 —	1-40
X	WO 98 06392 A (POZEN INC) 19 February 1998 (1998-02-19)	1,4-10, 21-23, 25-32
A	page 1-24; claims 1-15,18-20,23-34,37-52; examples —	33,35-38
X	WO 98 15275 A (ALGOS PHARM CORP) 16 April 1998 (1998-04-16)	1-3,5, 21,22, 29-33,36
A	page 14, line 28, paragraph 1.55 —page 15, line 22; claims 3,7,14,18 —	4,6,7, 35-37
		—/—

 Further documents are listed in the continuation of box G. Patent family members are listed in annex.

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